REMARKS

A. Rejections under 35 U.S.C §112, first paragraph are moot

Claims 33-37 and 49 are rejected under 35 U.S.C. §112, first paragraph, for containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. Applicant has cancelled claims 33-37 and 49 and therefore rendered the rejections moot.

B. Rejections under 35 U.S.C. §101 are overcome

Claims 1, 31-46, 48, and 49 are rejected under 35 U.S.C. §101 as not supported by either a specific, substantial, and credible asserted utility or a well-established utility.

The Office Action asserts that the specification "speculates that the DS-CAM polypeptide may be responsible for holoprosencephaly and/or several phenotypes of Down Syndrome" and "speculates that the DS-CAM molecule can be used to diagnose a variety of diseases, including mental retardation, holoprosencephaly, agenesis of the corpus callosum, or schizencephaly." The Office Action asserts that none of these proposed utilities is a "substantial utility", because the specification "does not provide any evidence to support any of these utilities beyond the knowledge that this gene maps to the region of the genome that is associated with Down Syndrome and this gene is a putative cell adhesion molecule." The Office Action further asserts that the proposed utilities are all speculative, and that they require further experimentation to reasonably confirm which, if any, are actual utilities of the DS-CAM molecules.

In addition, the Office Action asserts that the specification states "the nucleic acid molecules of the present invention are useful as probes for assaying for the presence and/or amount of a DS-CAM gene or mRNA transcript in a given sample" or "as primers and/or templates in a PCR reaction for amplifying genes encoding DS-CAM protein." The Office Action asserts that these utilities are non-specific because they are "applicable to a broad class of molecules, namely proteins and nucleic acids", and as such they are not sufficient to meet the utility standard of §101.

Applicant respectfully traverses. It is well established that the threshold for utility is not high. *Juicy Whip Inc. v. Orange Bang Inc.*, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir.

1999). An invention is "useful" under 35 U.S.C. 101 if it is capable of providing some identifiable benefit. *Id., citing Brenner v. Manson*, 383 U.S. 519, 148 U.S.P.Q. 689, 695 (1966). An applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. 101. See, for example, *In re Jolles*, 628 F.2d 1322, 206 U.S.P.Q. 885 (C.C.P.A. 1980); *In re Sichert*, 566 F.2d 1154, 1159, 196 U.S.P.Q. 209, 212-213 (C.C.P.A. 1977); *In re Langer*, 503 F.2d 1380, 183 U.S.P.Q. 288 (C.C.P.A. 1974); *In re Irons*, 340 F.2d 974, 144 U.S.P.Q. 351 (C.C.P.A. 1965). Unless there is reason to doubt the objective truth of the statements [contained in the specification] which must be relied on for enabling support, a specification's disclosure "must be taken as in compliance with the enabling requirement." *In re Brana*, 5 F.3d 1557, 34 U.S.P.Q.2d 1437 (Fed. Cir. 1995).

Role of DS-CAM in disease

Contrary to the assertions set forth in the Office Action, Applicant notes that the statements in the specification regarding DS-CAM function are not speculative in nature. For example, at page 10, lines 11-17, the specification states, "the expression pattern and the role of dendritic connections in cell body maintenance indicate that an increase in DS-CAM expression in Down Syndrome brain is responsible in part for the abnormalities of dendritic structure and decreased intersections seen at four months post-natal in Down Syndrome individuals."

Applicant further contends that one of ordinary skill in the art would reasonably correlate DS-CAM's genomic location, polypeptide structure, and expression pattern in fetus and adult animals with a role in Down Syndrome and other diseases associated with neural development.

According to the specification, DS-CAM maps to the small region of chromosome 21 that is associated with the Down Syndrome phenotype (specification page 43, lines 13-14). This region is also associated with holoprosencephaly (HPE1) and Hirschsprung's Disease (specification page 21, lines 14-16, and page 43, lines 24-27). Based on sequence homology, DS-CAM is a neural cellular adhesion molecule (N-CAM). N-CAMs are known to play an important role in neural development (page 2, lines 22-34). Mutations in the N-CAM CAM-L1 have been associated with several

neurological development disorders, including X-linked hydrocephalus, type 1 X-linked spastic paraplegia, and MASA syndrome, which displays agenesis of the corpus callosum (page 3, lines 1-7). In the fetus, DS-CAM is expressed primarily in the brain, with no expression in lung or liver (page 20, line 24-26). Neural crest cells express DS-CAM during migration (specification page 9, lines 16-19). DS-CAM expression continues post-natally in differentiating regions of the newborn brain (specification page 10, lines 3-7). The specificity of DS-CAM expression for the central nervous system and the timing of its expression to the period of neurite outgrowth in both central and peripheral nervous systems indicates a role for DS-CAM in early development and differentiation (page 9, lines 1-6). In the embryo, differentiated neurons express DS-CAM when they have finished migrating to their proper positions within the neuroepithelium (page 9, lines 12-15). Taken in combination, the information set forth in the specification would be sufficient to convince one of skill in the art that DS-CAM plays a role in neural development, Down Syndrome, and other neural development disorders. Thus, the use of the claimed nucleic acids in the treatment of Down Syndrome and related disorders constitutes a credible, specific, and substantial utility.

DS-CAM as a diagnostic marker

Applicant notes that the nucleic acids disclosed in the present application have a least one well-established utility and/or at least one credible, specific, and substantial utility. For example, the nucleic acids can be used as a diagnostic marker for conditions such as Down Syndrome and HPE1.

Down Syndrome is associated with trisomy 21. A subset of the features associated with Down Syndrome, including typical facial appearance, mental retardation, and congenital heart disease have been attributed to duplication of the 21q22 region, which lies between D21S267 and MX1/MX2 on chromosome 21 (specification page 43, lines 5-13). The present application discloses a novel gene, DS-CAM, which resides in this region (specification page 43, lines 13-14). The Ts65Dn mouse model of Down Syndrome also contains the chromosomal region containing DS-CAM, MMU16 (Pgk1-ps1 to MX1/2) (specification page 43, lines 14-19). The region of 21q22.2 from which DS-CAM maps is also part of the candidate region for HPE1

(specification page 21, lines 14-16). Deletion of this region has been linked to HPE1, which causes abnormalities of the corpus callosum and schizencephaly (specification page 21, lines 16-18).

A subject having Down Syndrome will display trisomy for the 21q22 region (specification page 43, lines 5-13), meaning that they will necessarily have three copies of the DS-CAM gene. A subject having HPE1 is likely to possess only one copy of the 21q22 region (specification page 21, lines 16-18), meaning that they will possess only one copy of the DS-CAM gene. The claimed nucleic acids can be used as hybridization probes to detect the number of DS-CAM genes in a given sample . By detecting the number of copies of the DS-CAM gene, these nucleic acids can be used to diagnose diseases such as Down Syndrome and HPE1. The claimed nucleic acids will be more accurate at diagnosing Down Syndrome than nucleic acids that bind to some other region of chromosome 21, because it is possible for a subject to display the Down Syndrome phenotype with trisomy of the 21q22 region only.

The specification specifically discloses the use of the claimed nucleic acids as probes, stating that they "can be labeled with a readily detectable substituent and used as hybridization probes for assaying for the presence and/or amount of a DS-CAM gene or mRNA transcript in a given sample" (page 12, lines 11-15). The specification also discloses a kit "for detecting mutations, duplications, deletions, rearrangements, and aneuploidies in chromosome 21 at locus q22.2 comprising at least one invention probe" (page 26, lines 2-4). In addition, the specification discloses a method and diagnostic system for diagnosing DS-CAM associated disease by detecting the amount of DS-CAM mRNA (page 44, line 17 – page 46, line 27).

M.P.E. P. 2107 (II) states "if at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility." This section goes on to state, "An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible." See, M.P.E.P. 2107.

DS-CAM maps in the 21q22 region of chromosome 21. Changes in this region (e.g., mutation, duplications, deletion, rearrangements, and aneuploidies) are directly associated with diseases such as Down Syndrome and holoprosencephaly (HPE1). The specification teaches the use of specific nucleic acid sequences as probes for detecting the presence of the DS-CAM gene and the number of copies of the gene (page 44, line 17 – page 46, line 27). In light of these facts, one of ordinary skill in the art would immediately appreciate that the claimed nucleic acids can be used to diagnose predisposition to diseases such as Down Syndrome and HPE1 by detecting the presence or number of copies of the DS-CAM gene.

"Credibility" is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. M.P.E.P. 2107. Diseases such as Down Syndrome and HPE1 are associated with trisomy or deletion of the 21q22 region, the same region that contains the DS-CAM gene. Given that DS-CAM maps in the 21q22 region whose changes (e.g., mutation, duplications, deletion, rearrangements, and aneuploidies) are directed associated with diseases such as Down Syndrome and holoprosencephaly (HPE1), one of ordinary skill in the art would readily appreciate that the detection of DS-CAM (its presence or amount) will inevitably predict the predisposition to diseases such as Down Syndrome and HPE1. In other words, a person of ordinary skill in the art would readily appreciate that the claimed nucleic acids could be used as probes to determine the presence or number of copies of the 21q22 region, making them useful diagnostic markers for conditions associated with deletions or trisomy in this region. It is difficult to imagine that the utility of DS-CAM as a diagnostic marker is not credible.

A "substantial utility" is defined as "real world" use. A utility is not considered "substantial" if it requires or constitutes carrying out further research to identify or confirm this "real world" use. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have "substantial utility" constitute a "real world" use. M.P.E.P. 2107.01. The claimed invention constitutes a "real world" use because the claimed nucleic acids are being used to diagnose diseases such as Down Syndrome and HPE1.

A "specific utility" is specific to the subject matter claimed. This is in contrast to a "general utility", which is applicable to a broad class of inventions. For instance, a claim to a nucleic acid whose use is described simply as "gene probe" or "chromosome marker" is not specific without disclosure of a specific DNA target. Likewise, a general statement of diagnostic utility, such as a method of diagnosing an unspecified disease, is not specific absent a disclosure of the condition to be diagnosed. M.P.E.P. 2107.01. In the present application, however, the claimed nucleic acids are used to diagnose specific diseases such as Down Syndrome and HPE1, and therefore the claimed inventions clearly meet the "specific utility" criteria.

In light of the foregoing, a person of ordinary skill in the art would immediately appreciate why the claimed invention is useful as a diagnostic marker for diseases such as Down Syndrome and holoprosencephaly based on the disclosure in the application. In addition, such a utility is specific, substantial, and credible. Accordingly, Applicant believes the specification meets the utility requirements of 35 U.S.C. 101 and respectfully requests that the rejections be withdrawn.

CONCLUSION

In view of the foregoing, it is submitted that the present claims are in condition for allowance. Accordingly, Applicant respectfully requests that a Notice of Allowance be issued.

Respectfully submitted,
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